

## REMARKS/ARGUMENTS

### *Claim Rejections - 35 U.S.C. § 101 and 35 U.S.C. § 112*

The Examiner has maintained the 35 U.S.C. § 101 rejection of claims 1-3:

"... under 35 USC § 101 because the claimed invention is directed to non-statutory subject matter..." The claims are drawn to methods, which do not result in the production of a concrete tangible and useful result. The "method of merging" merely combines groups of data about chemical structures, with no specific output of a result that meets the concrete, tangible and useful criteria."

The Examiner further notes that:

"The claims use unspecified data of unspecified structure, composition, or type in the merging process. ... The claims encompass the use of the structures of a non-specific (and non-identified) genus of compounds wherein the relationship between the structural features of the members and a given function have not been defined."

The Examiner has also rejected the claims under 35 U.S.C. § 112:

"...as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." The Examiner then goes on to note that the term "maximum diversity" and "minimum redundancy" are relative terms which render the claim indefinite.

Since the §101 rejection involves, in part, the same issues as the §112 rejection, Applicants will address both the §101 and §112 rejection together. First, Applicants will address the part of the §101 rejection that is not shared by the §112 rejection.

Applicants respectfully disagree with the Examiner's analysis of the claims especially in view of the teaching of the patent application. Applicant has taught that metric descriptors used to characterize molecules, and, in particular, molecules which have associated biological activities, must be "valid" to be of any use. By "valid" is meant that the descriptor "measure the chemical universe in such a way that similar structures (as defined by the descriptor) have substantially similar biological properties." (Specification page 25, lines 15-16.) That is, if the descriptor value assigned to molecule A is substantially the same as the descriptor value assigned to molecule B, the two molecules are highly likely to share the same biological activity. If the descriptor values are substantially different, the two molecules are not likely to share the same activity.

Besides teaching a method to determine whether a descriptor is valid, the specification also teaches what is meant by substantially the same or substantially different. The specification teaches that every valid descriptor has associated with it a unique "neighborhood distance" that is an inherent property of the descriptor. Two molecules whose descriptor values fall within the neighborhood distance are highly likely to share the same activity. Two molecules whose descriptor values fall outside the neighborhood distance are highly unlikely to share the same activity. Besides teaching a method of how to determine whether a descriptor is valid and its associated neighborhood distance, the specification teaches the application of the method to several descriptors and identifies those that are valid.

In the context of libraries of molecules which are to be screened in biological assays, it is important from both an economic and time perspective to minimize the number of samples

that have to be run through the assay. On the other hand, one does not want to miss a hit in the assay by not screening a broad enough sample of compounds. Assaying molecules that have similar structures and activities increases the number that need to be sampled. Thus, what is wanted is minimum redundancy in the sample set; that is, a minimum number of molecules which are so close in structure that they sample the same chemical space. Assaying one is essentially the same as assaying both as far as what can be learned. Essentially it is desired that the samples to be assayed be different enough that they cover different areas/volumes of chemical space. Assaying one is not the same as assaying both as far as what can be learned. This requirement is summed up in the notion of desiring as much chemical diversity among the samples as is possible within the library.

The method of the present invention utilizes knowledge of metric validity and the associated neighborhood distances to meet the above cited requirements in the context of combining two or more assemblies of molecules. Claim 1 deals with the situation where the molecules within the individual assemblies have already been determined not to be redundant. This is reflected in the preamble language: "...similar molecules in the assemblies having previously been identified and removed..." Claim 1 then describes the method steps necessary to obtain the optimal diversity among the molecules. Most importantly, the claim recites the use of a "molecular structural descriptor, validated as possessing a neighborhood property." Because of this requirement, Applicants submit that the Examiner's characterization of the claim as using "unspecified data of unspecified structure, composition, or type in the merging process" is incorrect. Applicants further submit that the use of a validated molecular structural

descriptor inherently defines the relationship between structural features and function contrary to the Examiner's assertion. The validated metric is utilized in the method to ensure that no two molecules are included in the merged assembly which lie within the neighborhood distance of each other. This is the requirement for an optimally diverse assembly.

Claim 3 describes a method for dealing with assemblies of molecules that still contain similar molecules; that is, there is redundancy in each assembly. These assemblies do not meet the requirement of the preamble of claim 1 that "...similar molecules in the assemblies having previously been identified and removed..." Therefore, the first part of the method of claim 3 (step a subparts 1-6) deals with removing redundant molecules from each assembly before merger of the assemblies. The removal of redundant molecules is accomplished by keeping only those molecules that are separated by a distance greater than the neighborhood distance for the metric descriptor being used. If two molecules lie within the neighborhood distance of one another, only one is kept. In this manner, the merged assembly is diverse and minimally redundant.

Applicants have examined the language of the claims and have amended the final wherein clause of claim 1 and 3 to reflect more precisely what is accomplished by the methods. Applicants understand the Examiner's concern reflected in both the §101 and §112 rejections that the terms "maximum" and "minimum" are relative. In view of the specification, Applicants still believe that these terms are properly understood in view of the discussion presented above. However, Applicants have amended the claims to more clearly define and reflect that which they wish to claim. In particular, in claim 1, the term "optimally" has been

inserted to replace "maximum." Antecedent basis for this term and its associated meaning is found in the specification section *Merging Libraries* beginning on page 98 and in particular on page 100, lines 4-7. Similarly, the term "minimum" has been replaced with the phrase "does not redundantly include molecules likely to share the same activity."

Applicants submit that, in view of the technology disclosed in the specification as discussed above and the amendments to the claims, the claims set forth a concrete, tangible, and useful result meeting all statutory requirements. The claims do not "manipulate abstract data to come to an abstract conclusion" as suggested by the Examiner. Rather the claims set forth a defined method of employing validated molecular descriptors that relate structure to function (activity) to characterize and merge assemblies of molecules for a specific purpose to a specific end. Finally, Applicants incorporate their remarks with respect to the requirements of 35 U.S.C. § 101 made in their office action response dated March 13, 2003.

For all the reasons set forth above, Applicants respectfully submit that they have adequately addressed all grounds for rejection raised by the Examiner and respectfully request that a timely Notice of Allowance be issued in this case.

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Respectfully submitted,

  
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